

Maternal and Neonatal Outcomes of Pregnant Women with COVID-19 in İstanbul, Turkey: A Single-center, Descriptive Study

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What is known on this subject?

The coronavirus caused many unknown pneumonia cases that were clinically similar to viral pneumonia in Wuhan, a city in the Hubei Province of China, in December 2019. On January 30, 2020, the World Health Organization announced that the new coronavirus was a public health emergency of international concern. The virus spread rapidly worldwide and the number of cases began to increase in the other countries in February 2020. The first case in our country was announced on March 11, 2020. Until this date, the number of cases detected in the world was 125.900, but now (June 2) is 6.378 M. Currently, knowledge on the epidemiology and clinical features of pneumonia in pregnancy caused by coronavirus disease-2019 (COVID-19) is limited. Therefore, sharing clinical and epidemiological data on COVID-19 infected pregnancy is crucial for improving perinatal outcome. Effective obstetric therapy is required in these pregnant women and is key to optimizing the prognosis for both mother and child. Care should be individualized in determining the time of delivery, evaluating the C-section indications, preparing the delivery room to prevent infection, choosing the type of anesthesia and managing the newborn. Birth and treatment experiences are limited for pregnant women who have had the disease in the last 3 months.

What this study adds?

In our study, we define the epidemiological, clinical, laboratory and radiological features, maternal and neonatal outcomes and treatment of pregnant women confirmed to have severe acute respiratory syndrome coronavirus-2 infection.

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ABSTRACT

Objective: This study aimed to define the approach to pregnant women with coronavirus disease-2019 (COVID-19) and to determine the maternal and neonatal consequences of the disease.

Material and Methods: Maternal and neonatal outcomes of COVID-19 pregnant women are illustrated by looking at the following parameters: Real-time reverse transcription polymerase chain reaction test, complete blood count, D-dimer and ferritin concentration, lymphocyte count, aspartate aminotransferase, C-reactive protein, and alanine aminotransferase level, neonatal umbilical blood gas analysis, admission to the neonatal intensive care unit (NICU), and lung computed tomography images.

Results: Forty-three trimester pregnant women with a diagnosis of COVID-19 were included in the study. The most common complaint at admission was cough (50%), and the most common accompanying finding was shortness of breath and fever. The delivery method was 34 patients cesarean section and 6 patients vaginal delivery. Two neonates were admitted to the NICU due to respiratory distress. There were no maternal or infant deaths. The patients were hospitalized for approximately 5 days.

Conclusion: To sum up, our study is a preliminary study and there is a need for studies involving a much larger number of patients in terms of clinical features and follow-up treatment of pregnant women with COVID-19. In this regard, long-term patient follow-up results will be extremely important.

Keywords: COVID-19, maternal and neonatal outcomes, pregnant, obstetrics and gynecology

Introduction

The coronavirus caused many unknown pneumonia cases that were clinically similar to viral pneumonia in Wuhan, in December 2019 (1). On the World Health Organization declared that the new coronavirus was a public health emergency of international concern on January 30, 2020. The virus spread rapidly worldwide and the number of cases began to increase in the other countries in February 2020 (2). The first case in our country was announced on 11, 2020. Until this date, the number of cases detected in the world was 125.900, but now (June 2) is 6.378 M (3). Currently, knowledge on clinical features and the epidemiology of pneumonia in pregnant women induced by coronavirus disease-2019 (COVID-19) is restricted. Therefore, sharing clinical and epidemiological data on COVID-19 infected pregnancy is crucial for improving perinatal outcome.

Effective obstetric therapy is required in these pregnant women and is key to optimizing the prognosis for both mother and child. Care should be individualized in determining the time of labor, appraising the C-section indications, choosing the type of anesthesia, arranging the delivery room to avoid infection and controlling the newborn. Birth and treatment experiences are limited for pregnant women who have had the disease in the last 3 months (4).

Our research aimed to define the clinical, laboratory, epidemiological and radiological features, maternal and neonatal outcomes and treatment of pregnant women confirmed to have severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection.

Material and Methods

This retrospective, single-center study was conducted at University of Health Sciences Turkey, Istanbul Kanuni Sultan Suleyman Training and Research Hospital, Turkey, between April and May 2020. The study protocol was approved by the University of Health Sciences Turkey, Bakirkoy Dr. Sadi Konuk Training and Research Hospital Ethics Committee and registered with ClinicalTrials.gov (NCT04337320) (decision no: 2020-09, date: 30.04.2020).

Our study criteria included pregnant women between 18 and 45 years old with a history of COVID-19-positive polymerase chain reaction (PCR) result. Patients with COVID-19-positive PCR who used systemic drugs as well as women with other endocrine and/or autoimmune disorders, pregnant women who had underlying lung disease were excluded from the study.

The demographic data of participants, including age, gravidity, parity, gestational week at admission were recorded. The samples from each patient were obtained to determine the complete blood count, alanine aminotransferase (ALT), C-reactive protein (CRP), aspartate aminotransferase (AST) levels, lymphocyte account and the concentrations of ferritin and D-dimer of blood. Simultaneously, neonatal umbilical blood gas analyses were also examined. Real-time reverse transcription-PCR test was applied to upper respiratory tract swab samples of all patients. We also requested lung computed tomography (CT) from all patients, except for 4 patients who did not wish to undergo any imaging tests. Six of the forty patients had normal vaginal delivery, others were delivered by the C-section and all newborn infants were admitted to the neonatology department for separation from the mother and for blood and PCR tests.

The primary outcome of our study was to compare maternal and neonatal results in pregnant women with a history of COVID-19-positive PCR result.

Statistical Analysis

Data analysis was performed by the SPSS version 20 for Windows (SPSS Inc., Chicago, IL). Continuous variables were expressed using means with standard deviations and categorical variables were expressed as numbers (%).

Results

Forty pregnant women with COVID-19 were included in the study. The demographic information of the patients is shown in Table 1. Two patients had a history of chronic disease (type 2 diabetes mellitus and hypothyroidism).

Most of the patients presented with cough complaints (50%). The most common symptoms accompanied by cough were fever and shortness of breath. A significant number of patients were asymptomatic (42.5%). While 15 patients needed nasal oxygen support during their hospitalization, 2 of our patients were hospitalized in the intensive care unit (ICU) due to serious respiratory problems. We divided the patients into groups according to the stage of CT findings. We detected 10 patients with mild involvement, 11 patients with moderate involvement and 8 patients with severe involvement. Lung CT findings and the clinical features of the patients are summarized in Table 2.

Laboratory findings of the pregnant on admission, such as complete blood count, coagulation tests, liver function tests, ferritin and CRP, were examined (Table 3).

Thirty-four of the patients had a C-section and six of them had a vaginal delivery. A patient with a previous C-section had severe AST (1560 U/L) and ALT (435 U/L) levels. Oxygen saturation under oxygen support was 94%. She had tachycardia (130 beats per minute) and shortness of breath. When she was

36 weeks of pregnancy, the decision was made by cesarean delivery. Four babies needed a neonatal ICU. Obstetric and neonatal characteristics are demonstrated in Table 4.

Forty-five percent of the patients received only hydroxychloroquine treatment. One patient was followed up without treatment. Low-molecular-weight heparin treatment (LMWH) was started for all patients. Patients with a D-dimer value above 2 mg/L were administered LMWH twice daily. The treatment options are shown in Table 5.

Discussion

The disease spread in our country in April and May. So far, 165.555 cases and 4.585 deaths have been reported in our country (5). This study is a descriptive study reporting the maternal and neonatal results of pregnant women with COVID-19 from a centre with an annual birth rate of more than 10.000.

This article reports the maternal and fetal results of 3rd trimester pregnant women who applied with COVID-19 in a tertiary center working as a pandemic hospital. 85% of patients gave birth by C-section. There was no maternal-fetal mortality or serious morbidity. Cough was the most common symptom, and 42.5% of patients were asymptomatic. As a general treatment approach of the country, the treatment was started by providing hydroxychloroquine within a short time after diagnosis.

Coronaviruses (CoV) are a major family of viruses that cause a diversity of illnesses by the common cold to more serious diseases such as SARS-CoV-2 and the middle east respiratory syndrome. Human beings can also be infected by inhalation of droplets scattered from the respiratory tract of the sick individuals or by contact with the surfaces contaminated with these aerocoles (6). Eighteen of our patients (45%) had a contacts with people who had a history of the disease.

Table 1. Demographic characteristics

Demographic characteristics	Study group (n=40)	Minimum - maximum	95% CI
Age	27.7±6.6	18-45	25.6-29.9
Gravidity	2.5±1.5	1-8	2.0-2.9
Parity	1.2±1.4	0-6	0.7-1.7
Gestational week of admission	37±2.7	29-41	36.1-37.9
Previous C-section (n, %)	9 (22.5%)	-	-
Chronic disease		-	-
Type 2 DM (n, %)	1 (2.5%)		
Hypothyroidism	1 (2.5%)		
Previous contact with COVID-19 patient	18 (45%)		

CI: Confidence interval, DM: Diabetes mellitus, COVID-19: Coronavirus disease-2019

Current evidence suggests that the severity of disease among pregnant women after COVID-19 infection is similar to non-pregnant adult COVID-19 cases, and there is no data showing that infection with COVID-19 during pregnancy has a negative effect on the fetus. Although rare, intrauterine transmission of SARS-CoV-2 has been reported (7). In our study, no vertical transition was detected as no infant had a positive PCR test.

In 2002-2003, there was a high maternal mortality rate in the SARS-CoV-1 outbreak (8). However, there has not been a similar situation in SARS-CoV-2 yet. However, more studies are needed on this subject. Looking at the current studies, it seems difficult to make clear comments (9,10). In Turkey, as of June 2, the overall mortality rate of the disease is 2.76%, and there

are no published articles showing maternal mortality rates in pregnant women with COVID-19 (5). Similarly, no maternal and fetal deaths have been observed in our hospital too.

In terms of clinical findings in patients, the common symptoms at baseline were cough, fever, and difficulty breathing, and the rate of asymptomatic patients was 22 (11,12). Similar to current studies, laboratory tests were observed as low lymphocyte count, increased CRP and D-dimer (13).

The relatively high mortality of COVID-19 is making people feel anxious. Most of the women had C-section in our study, similar to the literature (14). The most common C-section indication was maternal request. This was followed by difficulty breathing and anxiety.

Table 2. Clinical features of the patients

Clinical features of the patients	Study group (n=40)	Minimum - maximum	95% CI
Symptom (n, %)		-	-
Asymptomatic	17 (42.5%)		
Fever	10 (25%)		
Cough	20 (50%)		
Shortness of breath	10 (25%)		
Fatigue	2 (5%)		
Anosmia	2 (5%)		
Body temperature (°C)	36.5±0.7	35.5-39	36.3-36.7
Heart rate (bpm)	94.7±15.1	69-136	89.8-99.5
Oxygen saturation	96.2±2.8	88-100	95.3-97.1
Systolic blood pressure (mmHg)	114.9±12.8	90-142	110.8-119
Diastolic blood pressure (mmHg)	70.7±9.9	50-89	67.5-74
Need for oxygen therapy	19 (47.5%)		
Need for ICU (n, %)	2 (5%)		
Lung CT findings			
Refused investigation	4 (10%)		
No involvement	7 (17.5%)		
Mild involvement	10 (25%)		
Moderate involvement	11 (27.5%)		
Severe involvement	8 (20%)		

CI: Confidence interval, CT: Computed tomography, ICU: Intensive care unit

Table 3. Laboratory findings at admission

Laboratory findings on admission	Mean ± SD (n=40)	Minimum - maximum	95% CI
Hemoglobin (gr/dL)	11.4±1.4	8.4-15.3	11-12
Hematocrit (%)	34.3±3.5	25.7-45.2	33.2-35.4
Platelet count (10 ³ /μL)	222±70	102-468	200-245
D-dimer (mg/L)	3.1±2.7	1-14.9	2-3.9
Ferritin (ng/mL)	50.8±57	9.4-355	32-69.4
AST (U/L)	67.2±242	12-1560	-10.3-145
ALT (U/L)	32.3±69	5-435	10.2-54.4
CRP mg/L	31.4±52	0.7±292.6	14.6-48.3
Lymphocyte count (10 ³ /μL)	1.8±1.5	0.5±8.5	1.3-2.3

CI: Confidence interval, SD: Standard deviation, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C-reactive protein

Table 4. Obstetric and neonatal characteristics

Obstetric and neonatal characteristics	Study group (n=40)	Minimum - maximum	95% CI
Delivery route (n, %)		-	-
C-section	34 (85%)		
Vaginal	6 (15%)		
C-section indications (n, %)			
Multiple pregnancy	2 (5.8%)		
Previous C-section	9 (26.4%)		
Maternal hypoxia	3 (8.8%)		
Maternal request	15 (44.1%)		
Malpresentation	2 (5.8%)		
Fetal distress	3 (7.5%)	-	-
Premature birth (n, %)	15 (37.5%)		
Birth weight (gram)	2955±656	1255-4000	2745-3165
5 th minute APGAR score	8.8±0.6	6-9	8.6-9
Umbilical cord pH	7.38	7.2-7.4	7.37-7.39
Need for NICU	4 (10%)	-	-
Positive neonatal PCR test	0		

CI: Confidence interval, NICU: Neonatal intensive care unit, PCR: Polymerase chain reaction

Table 5. Treatment options

Treatment options	Study group (n=40)	Minimum - maximum
None- observation (n, %)	1 (2.5%)	-
LMWH	40 (100%)	
Hydroxychloroquine (n, %)	18 (45%)	
Hydroxychloroquine + azithromycin (n, %)	7 (17.5%)	
Hydroxychloroquine + azithromycin + oseltamivir (n, %)	7 (17.5%)	
Hydroxychloroquine + lopinavir/ritonavir (n, %)	4 (10%)	
Hydroxychloroquine + azithromycin + lopinavir/ritonavir (n, %)	3 (7.5%)	2-12
Duration of hospitalization (days)	5.4±2.5	

LMWH: Low-molecular-weight heparin treatment

Lung CT findings are important for the diagnosis of pneumonia in pregnant women with COVID-19. In patients who had mild involvement in CT, multiple patchy frosted glass areas are peripherally located rather than parenchyma, and lesions increased as the disease progresses. According to the study by Li et al. (15), extensive pulmonary consolidations are observed in cases of severe involvement, “white lungs” may appear on the radiogram, but pleural effusion is rare.

For treatment, hydroxychloroquine is usually used along with a second-generation macrolide. There is not enough data to know if it plays a role in treatment, but it is widely used. It can also cause QT prolongation and ventricular arrhythmias, which may pose a certain risk of critical patients (1,16). Among the 40 patients we examined, no cardiac side effects related to drug use were observed. Additionally, heparin has been suggested to be added to treatment by some specialized consensus due to the risk of disseminated intravascular coagulation and venous thromboembolism. Heparin

treatment has been related to good prognosis, mostly in severe COVID-19 cases with high D-dimer concentrations (17). Lopinavir, another treatment option, is a protease inhibitor used to treat HIV along with ritonavir. In one of a randomized study with 199 patients by Cao et al. (18), 99 of these patients were evaluated in the group receiving lopinavir-ritonavir and 100 in the standard care group. According to this study, it was observed that there was no additional benefit of lopinavir-ritonavir treatment beyond standard care in adult patients diagnosed with heavy COVID-19. Oseltamivir is an approved neuraminidase inhibitor for treating influenza. Since the epidemic in China occurred during the peak season of influenza, oseltamivir was added to the treatment of patients. In fact, this agent plays no role for treating COVID-19 after influenza (19). We applied LMWH and hydroxychloroquine to pregnant women as standard treatment. We observed one of our patients without treatment because she was asymptomatic and laboratory values were normal. Initially,

we added oseltamivir to the treatment of 7 patients because of the seasonal period. We used lopinavir/ritonavir treatment in patients who needed oxygen therapy and had severe involvement findings on lung CT. We have created our treatment algorithm according to the “COVID-19 guide”, which is updated regularly by our health ministry since the disease first appeared in our country. Changes in treatment arise from this (20).

Study Limitations

The most important advantage of this study is that it is single-centered and covers 40 patients. Similarly, the number of patients was generally kept lower in other articles planned. Nevertheless, this study has some limitations. All patients included were in the third trimester, it is still unknown how the fetuses of pregnant women whom infected with COVID-19 in the first and second trimesters will be affected. More studies are needed to the maternal and neonatal long-term results of the pandemic.

Conclusion

According to our experience, the clinical features of pregnant women with COVID-19 in the third trimester are similar compared to non-pregnant adults. According to our study, no vertical transition was observed. Maternal and fetal results seem favorable to non-COVID-19 pregnant women. Long-term results and comparative studies are required.

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Ethics

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences Turkey, Bakirkoy Dr. Sadi Konuk Training and Research Hospital Ethics Committee and registered with ClinicalTrials.gov (NCT04337320) (decision no: 2020-09, date: 30.04.2020).

Informed Consent: Informed consent was obtained from the patients.

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Authorship Contributions

Surgical and Medical Practices: İ.P., M.Ç., Concept: M.A.T., Design: M.A.T., Data Collection or Processing: P.Y.B., A.B., O.K., Analysis or Interpretation: A.A., Literature Search: M.A.T., O.K., S.Y.S., Writing: İ.P., M.A.T.

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